REMARKS

Claims 28, 29, 32-35 and 47-49 are currently pending in the application. Claims 28, 29, 33, 34, 47 and 48 have been amended. Reexamination and reconsideration of the application as amended is requested.

The Examiner has rejected claims 28 and 33-35 under 35 U.S.C. § 112, second paragraph as indefinite. The Examiner asserts that claim 28 is indefinite over "homologous with the zinc finger domains" because it is not clear as to which zinc finger domains the nucleic acid is homologous to. Claim 28 has been amended to recite homology in terms of the protein produced rather than in terms of the nucleic acid itself. In addition, the resulting protein has been limited to those encoded by the PLAG1 gene having a cDNA sequence as disclosed in the present specification. The Examiner also asserts that it is not clear whether the 25% of the polypeptide that is not identical to the polypeptide sequence of the PLAG1 in the region from zinc fingers 4 to 7 retains the function of the unaltered protein. Claim 28 has been amended to recite the function of the protein to clarify that nonidentical protein retains the function of the unaltered protein. The Examiner maintains that claims 33-35 are indefinite because the recitation of "a first one" and "a second one" is unclear as to what "ones" are being referred to. Claims 33 and 35 have been amended to remove references to "a first one" and "a second one" and to refer to "said oligonucleotide, polynucleotide or gene."

The Examiner has maintained the rejection of claims 28-29, 32-35, and 47-49 under 35 U.S.C. § 112, first paragraph, for inadequate written description. The Examiner asserts that the "at least a part" terminology used in the claims encompasses a large number of genes and sequences that are not described or disclosed. The Examiner also asserts that the specification fails to adequately describe the various nucleotide variations, such as substitutions, insertions, deletions, nonsense or frameshift mutations that are encompassed by the gene. The references in claims 33, 47 and 48 to a "part" have been amended to read on at least one exon, thus

characterizing the claimed species in terms of structure and a function. In addition, claims 33, 47 and 48, and therefore all dependent claims, as amended, now refer to the PLAG1 gene. A description of the gene, including genomic organization and regulatory regions such as exons, and a disclosure of the nucleic acid of the nucleotide sequence of the cDNA of PLAG1 are provided on p. 41 and Figs. 3A and 4A of the specification. Therefore, the claims as amended do not embrace the nucleotide variations described by the Examiner, or the genes and sequences that the Examiner maintained were not described or disclosed. For these reasons, the rejection of claims 28-29, 32-35, and 47-49 for inadequate written description is believed to have been overcome.

The Examiner has maintained the rejection of claims 28-29, 32-35, and 47-49 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner asserts that the specification, while being enabling for the cDNA sequence of the PLAG1 gene, does not reasonably provide enablement for an isolated nucleic acid wherein the nucleic acid is one of an oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7. As noted previously, the reference in claims 33 and 47 to a "part" has been changed to a reference to an "exon", which is a disclosed component of the genomic organization of the PLAG1 gene. The requirement in claims 33 and 47 that an exon be present in the claimed species provides sufficient limitation to the number of nucleotide variations encompassed by the claims, as well as conforming the claimed subject matter to the support found in the specification.

The Examiner also asserts that the specification does not reasonably provide enablement for a nucleic acid having homology with the zinc finger domains of the PLAG1 gene or the complementary strand thereof, including modified, degenerate, or elongated versions of

both strands. Claim 28 has been amended to refer to a nucleic acid which encodes a protein which is homologous to the protein encoded by the PLAG1 gene. The present specification contains a description, at p. 41 lines 10-25, of the identification of at least one additional human gene by alignment of ESTs resulting in a contiguous sequence of about 1 kb comprising an open reading frame with a homology at the amino acid level of about 75% in the region encoding zinc fingers 4 to 7 of the PLAG1 gene of the present invention.

The Examiner further asserts that the specification does not reasonably provide enablement of a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof. Claim 33, the only independent claim containing a reference to at least one part of the CTNNB1 (β catenin) gene, has been amended to refer to at least one exon of the CTNNB1 (β catenin) gene. Support is found in Figs. 6A and 6B, and in the figure legend on pages 52-53 of the specification, which show CTNNB1/PLAG1 and PLAG1/CTNNB1 fusion transcripts, i.e. nucleic acids comprising at least one exon of the PLAG1 gene. These fusion transcripts correspond with RT-PCR transcripts found in primary pleomorphic adenomas, using the protocol and primers as described at point 2, "Materials and methods" starting from page 35 to 39, and more specifically at point 2.7, "RT-PCR." The nucleic acid need not encode a functional protein, because at least one function of the claimed nucleic acid is its use in diagnostic applications.

For these reasons, the rejection of claims 28-29, 32-35, and 47-49 for lack of enablement is believed to have been overcome.

The Examiner has rejected claim 33 under 35 U.S.C. § 102(b) as anticipated by Kraus et al. (*Genomics* **23**:272-274 (December 1994)) (hereinafter "Kraus"). The Examiner asserts that, because the claims are drawn to at least a part of the PLAG1 gene and at least a part of the CTNNB1 gene, any fusion of at least a part (i.e., one or more nucleotides) of PLAG1 and CTNNB1 would be considered prior art. The Examiner also asserts that Kraus teaches this embodiment in the paragraph bridging p. 272, column 2 and p. 273, column 1, and Fig. Legend

1. Claim 33 has been amended to state that each oligonucleotide, polynucleotide or gene must contain at least one entire exon. In addition, claim 33 as amended is restricted to the PLAG1 gene of the present invention. Kraus does not describe fusions of CTNNB1 with at least one exon of the PLAG1 gene. For these reasons, the rejection of claim 33 over Kraus is believed to have been overcome.

The Examiner has rejected claims 33-35 under 35 U.S.C. § 102(a) as anticipated by Nollet et al. (*Genomics* **32**:413-424 (March 1996)) (hereinafter "Nollet"). The Examiner asserts that Nollet discloses the embodiment of claim 33. The Examiner asserts that Nollet discloses a macromolecule wherein the derivative is a nucleic acid including a gene, or a derivative thereof, isolated by using at least part of a T-gene as one of a probe or primer, corresponding to the embodiment of claim 34. The Examiner also asserts that, with respect to claim 35, Nollet teaches that the derivative is labeled. Claim 33 as amended reads on a macromolecule comprising a fusion containing at least one exon of the PLAG1 gene and at least one exon of the CTNNB1 gene. Nollet does not describe fusions of CTNNB1 with at least one exon of the PLAG1 gene. Claim 34, as amended, no longer contains option (d); therefore, the teachings of Nollet no longer correspond to the embodiment of claim 34. For these reasons, the rejection of claim 33-35 over Nollet is believed to have been overcome.

In view of the above amendments and remarks, it is believed that the claims are in condition for allowance. Reconsideration of the rejections is requested. Allowance of claims 28, 29, 32-35 and 47-49 is respectfully requested.

Respectfully submitted,

WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.

By _____

Barbara E. Johnson
Registration Number 31,198
Attorney for Applicants
700 Koppers Building
436 Seventh Avenue
Pittsburgh, PA 15219-1818
Telephone: (412) 471-8815
Facsimile: (412) 471-4094
E-mail: webblaw@webblaw.com

MARKED-UP VERSION OF THE CLAIMS

28. (Three Times Amended) [The] A nucleic acid [as claimed in claim 47] in isolated form, wherein the nucleic acid encodes a protein which is homologous [with the zinc finger domains of] to the protein encoded by the *PLAG1* (pleomorphic adenoma gene 1) gene [the nucleotide sequence of which] , wherein the cDNA sequence corresponding to said *PLAG1* gene is depicted in figure 4A (SEQ ID NO: 116), [or a complementary strand thereof,] and wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to [a] the polypeptide sequence [of] encoded by *PLAG1* in the region from zinc fingers 4 to 7 as represented in SEQ ID NOs 120 to 123, or a complementary or antisense version of the nucleic acid.

29. (Four Times Amended) The nucleic acid as claimed in claim 47, comprising the nucleotide sequence of the *PLAG1* gene as depicted in figure 4A (SEQ ID NO: 116), or a complementary [strand thereof] or antisense version of the nucleic acid.

33. (Four Times Amended) A macromolecule comprising a nucleic acid in isolated form, comprising a fusion of at least two of an oligonucleotide, a polynucleotide and a gene, wherein at least a first one of said oligonucleotide, polynucleotide or gene comprises a nucleotide sequence of at least [part of a T-gene selected from the group] one exon consisting of the [*PLAG*] *PLAG1* (pleomorphic adenoma gene 1) [subfamily of zinc finger protein genes] gene, and wherein at least a second one of said oligonucleotide, polynucleotide or gene comprises at least [part] one exon of the *CTNNB1* (ß catenin) gene, or complementary or antisense versions of the nucleotide sequence.

34. (Twice Amended) The macromolecule as claimed in claim 33, wherein the nucleic acid is selected from the group consisting of:

a) a transcript corresponding to the nucleic acid;

b) cDNA corresponding to the nucleic acid; and

c) sense or antisense DNA corresponding to the nucleic acid [;] .

[d) a nucleic acid including a gene, or a derivative thereof, isolated by using at least part of a T-gene as one of a probe or primer;

e) a protein encoded by the nucleic acid: and

f) antibodies, or derivatives thereof, directed to the nucleic acid, the transcript, the cDNA and the protein.]

47. (Four Times Amended) A nucleic acid in isolated form, wherein the nucleic acid is one of an oligonucleotide, a polynucleotide and a gene comprising a sequence of at least [part] one exon of the *PLAG1* (pleomorphic adenoma gene 1) gene, or the complementary sequence or antisense version of the nucleic acid; wherein [a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide sequence of *PLAG1* in the region from zinc fingers 4 to 7] said *PLAG1* gene encodes a protein comprising at least one of the zinc fingers 1 to 7 represented by the sequences as represented in SEQ ID NOs 117 to 123.

48. (Once Amended) A macromolecule comprising a nucleic acid in isolated form, comprising a fusion of at least two of an oligonucleotide, a polynucleotide and a gene

having a nucleotide sequence of at least [part of an intron or] one exon of the *CTNNB1* gene, or the complementary sequence or antisense versions of the nucleotide sequence.